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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,799	05/01/2001	Richard T. Wyatt	157/48457	2915

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/446,799	WYATT ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5 and 7-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 14
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-4, 6 and 14 in Paper No. 13 is acknowledged. The traversal is on the ground(s) that restriction was made by the previous office action is not proper based on the burden of the search and obviously all the all members in group I is in the same class and subclass. Furthermore, there is no basis for the restricting because the invention as claimed includes the alteration in both the CD4bs epitope and CD4I epitope. This is not found persuasive because the limitations of the reserved epitope and removed glycosylation sited are clearly recited in the claim 1 and 2, and they are not decided or divided by the office. For example, the maintained discontinuous conserved epitope is a CD4bs or a CD4i as cited in claim 2. The class and subclass are not only criteria for the restriction. The polypeptides of gp120 with different kind of modification exhibit different structural and functional characteristics and the source for conducting a complete search for one patent per one application is rather imitated, it would constitute a serious burden for office to search or examine fore than one patentable distinctive subject matters in the regular office practice.

2. Regarding to the further election of the glycosylation sites, since the elected claims does not include any particular modified position, the further election of the glycosylation sites on a particular amino acid residues are withdrawn.

3. Therefore, the claims 1-4, 6 and 14 within the scope of HIV-1 and CD4bs are considered before the examiner.

4. Applicants are reminded to amend the claims 1, 3 and 4 within the scope of HIV1 and CD4bs for reflecting the examination on the merits.

5. Applicants are request to cancel the claims 5, 7-13 drawn to the non-elected group.

Priority

6. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (e) as follows:

7. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-4, 6 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 is unclear for defining which modified gp120 polypeptide is. If Applicants wish to claim a particular modified gp120, the claim should point out a precise structure with a defined sequence identification number because HIV contains many clades and they differ in structure. The reasons for this indefinite rejection is described as follow:

1). The recitation of "at least" used here is a relative word, which cannot define what the precise structure of claimed polypeptide is;

2). The metes and bounds of "portion of at least two conserved regions" are not defined because HIV gp120 has 5 conserved regions, which range in different lengths and sequence structures. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of "portion" is. If applicants wish to deletion a particular portion of the conserved regions, the claim should point out which portion of the regions should be deleted precisely;

3). The CD4 biding site and chemokine biding site are not defined. The claim is interpreted in the light of the specification; however, the specification does not give the definitions of the biding sites are referred to. Moreover, there are many chemokines are in the art; the claim fails to define which chemokine is intended. The claim is interpreted in light of the specification; however, the limitation of the specification cannot read into the claim. If Applications wish to claim a particular site for a particular chemokine, please amend the claim to the precise site for the chemokine that is intended. Moreover, HIV

gp120 comprise many CD4bs spreading among a couple hundreds of amino acid sequence, claim should point out which CD4bs is intended.

4). A discontinuous conserved epitope is not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of a discontinuous conserved epitope is and which epitope of HIV gp120 is intended.

This affects the dependent claims 2-4 and 14.

11. Claim 6 is indefinite in that the metes and bounds of hydrophobic amino acid residues are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of hydrophobic amino acid residue is. Moreover, the claim is unclear for defining which a defined turn structure is. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of a defined turn structure is. If Applicants wish to claim a gp120 polypeptide that is modified by introducing a Pro residue in the gp120 genome, please amend the claim to indicate precisely where the pro is introduced.

12. Claim 14 is unclear in that the metes and bounds of pan-reactive T-cell helper epitopes are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of pan-reactive T cell-helper epitope is. If Applicants wish to claim a particular epitope, please amend the claim to a particular epitope. In addition, claim 14 is confusing for using a relative word of "at least" , which fail to define what the precise mutated structural of the claimed polypeptide is. Since there is no given upper limitation of the claimed components, the claims are considered as indefinite.

13.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-4, 6 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making some recombinant HIV gp120 according to the state of art (not the example of the specification of the present application because the specification does not present to produce any or all modified HIV gp120 molecule), wherein the HIV gp120 can be modified in certain position of the glysocylation site near the discontinues epitope of CD4bs, or deletion of the variable regions V1, V2 and/or V3, which enable for the better exposure of the hidden CD4bs in the interface of HIV gp120 molecule, does not reasonably provide enablement for having a modified HIV gp120 molecule, which is modified by alternating any or all glycosylation sites near the CD4bs and maintaining only at least any or all portion of two conserved regions, wherein t he said molecule is enabled for maintaining the 3-dimesional structure of the discontinuous conserved epitope of the wild-type gp120, such as CD4bs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of the scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) & 2). State of art and unpredictability.

The method for making a modified HIV gp120 are well known in the art. However, the field is still unpredictable because change certain amino acids in the HIV gp120 molecule can dramatically effect the ability of gp120 protein binding to CD4 as taught by Sodroski et al. (US Patent NO. 5,817,316, lines 15-29 on col. 3) and Olshevsky et al. (J. Virol. 1990, Vol. 64, pp. 5701-5707, see entire document). Sometimes, single amino acid changes in HIV envelope affect viral tropism and receptor binding as

evidenced by Cordonnier et al. (Nature 1989, Vol. 340, pp. 571-574 see entire document).

HIV gp120 contains 5 conserved regions, some amino acid residues located in these regions are indispensable for maintaining the CD4 binding site (CD4bs) reorganization as taught by Thali et al. (J. Virol. 1992, Vol. 66, pp. 5635-5641, see lines 7-26 on page 5636 of col. 2). The specification should be point out which portion can be deleted and which portion should be maintained precisely.

HIV gp120 contains 24 glycosylation sites. However, not every site mutation and not every kind of mutation in the same site are enable for maintaining the 3-dimensional structure of the discontinuous epitope of CD4bs. The random alteration of the glycosylation sites may affect the CD4 receptor binding sites as disclosed by Ho et a. (P.N.A.S. USA, 1991, Vol. 88, pp. 8949-8952, see entire document) and Lekutis et al. (Journal of Acquired Immune Deficiency Syndromes 1992, Vol. 5, pp. 78-81). The specification does not teach which site should be altered and how it should be altered precisely.

3) & 4). Number of working examples and amount of guidance.

Applicants describe some hypothesis for making a recombinant HIV gp120 based on the prior art that teaching HIV-1 gp120 contains some CD4bs epitope, CD4i epitope, and the 2G12 epitope, and where each of the epitops are possibly located.

However, the specification has no working examples of the claimed invention. For example, specification does not have a disclosure that any or all modified HIV gp120 by alteration of the glycosylation sites near the CD4bs is enabled for maintaining the 3-dimesional structure of the discontinuous epitope of CD4bs, where a Pro residue is introduced; how to increase the hydrophobicity of the gp120 interface; how to filing the cavity of the gp120; which Pan-T-cell epitope is introduced into the polypeptide; how it is introduced; where it is introduced; where a disulfide bonds are introduced into the molecule and how a modified HIV gp120 is tested by for its function. Overall, there is no any modified HIV gp120 has been made by the hypothetic description.

Applicants present no guidance how the skilled artisan would address and overcome the art-recognized problems as described supra.

5) Scope of the claims.

The scope of the claimed invention read broadly on any or all modified HIV gp120.

6) & 7). Nature of the invention and level of the skill in the art..

The nature of the invention is involves a high technique for modifying HIV gp120, which enable the modified polypeptide to maintain the overall 3-dimesional structure of a discontinuous conserved epitope of a wild-type gp120. This require a high technology and lot of non-routing work to test every mutation for its binding ability for the CD4.

Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-4 and 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 09/446,820. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of claimed inventions are overlaping.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 1-4 and 6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 and disclosure of the specification of U.S. Patent No. 5,817,316. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claimed inventions are overlapping..

In the instant case, Sodroski et al. disclose an immunogenic gp120 polypeptide from HIV-1, HIV-2 and SIV comprising the conserved regions, which has at least one of

variable regions V1-V3 deleted and replaced by a linker sequence, wherein the linker sequence comprising one to eight amino acids and said linker sequence maintains the overall 3-dimensional structure of the gp120 by permitting turns in the tertiary structure. The linker sequence in comprised of amino acid residues selected from the group consisting of Pro. Glu. And Ala (claims 1-11). The mutated gp120 polypeptide has different sequence structure compared to the wild type, therefore, the glycosylation sites are altered compared with the original sequence. The removal of the variable regions increases the exposure of the discontinuous epitope but maintain its 3-dimesional structure of discontinuous conserved epitope of the wild-type gp120, CD4 binding activity (se entire document, especially, the lines 49-60 on col. 6).

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

21. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Sodroski et al. (US Patent No. 5,817,316A).

22. Sodroski et al. disclose an immunogenic gp120 polypeptide from HIV-1, HIV-2 and SIV comprising the conserved regions, which has at least one of variable regions V1-V3 deleted and replaced by a linker sequence, wherein the linker sequence comprising one to eight amino acids and said linker sequence maintains the overall 3-dimensional structure of the gp120 by permitting turns in the tertiary structure. The linker sequence in

comprised of amino acid residues selected from the group consisting of Pro. Glu. And Ala (claims 1-11). The mutated gp120 polypeptide has different sequence structure compared to the wild type, the glycosylation sites are altered compared with the original sequence. The removal of the variable regions increases the exposure of the discontinuous epitope but maintain its 3-dimesional structure of discontinuous conserved epitope of the wild-type gp120, CD4 binding activity (se entire document, especially, the lines 49-60 on col. 6). Therefore, the claims invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

24. Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by Cao et al. (J. Virol. 1997, Vol 71, pp. 9808-9812).

25. Cao et al. teach a modified HIV gp120 glycoprotein, wherein the gp120 glycoprotein comprise the conserved regions and is modified in the variable regions V1-V2 and/or V3. The mutated polypeptide of HIV gp120 exhibits a better exposure of several discontinuous conserved gp120 epitopes and the exposure of the CD4 binding site (CD4bs). The ΔV1/2 envelope glycoprotein contains a deletion of gp120 residues 128-194. The ΔV3 envelope glycoprotein contains a deletion of gp120 residues 303-323. The ΔV1/2/3 envelope glycoprotein contains both above deletions (see lines 4-20 on col. 2, page 9808). These deletions change the glycosylation site as compared with e original sequence of wild-type gp120, but modified polypeptide maintains CD4 binding activity. Therefore, the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

26. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

27. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Ho et al. (J. Virol. 1991, Vol. 65, pp. 489-493).

28. Ho. et al. disclose a synthetic and unglycosylated recombinant envelope peptide of HIV gp120 expressed by E Coli or Saccharomyces cervisae, wherein the peptide comprises a CD4 binding site (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

29. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Wyatt et al. (J. Virol. 1997, Vol. 71, pp. 9722-9731).

30. Wyatt. et al. disclose several recombinant envelope protein of HIV gp120 mutated only comprising the deletion of certain amino acid residue located in 128-194, 298-329 in C1 and V1/2/3 regions, wherein the peptide still contains a conformation epitope and CD4 binding site (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

31. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Binley et al. (AIDS RESEARCH AND HUMAN RETROVIRUSES 1997, Vol. 14, p. 191-198).

32. Binley et al. disclose a recombinant envelope protein of HIV gp 120 comprising the conserved regions and variable regions V1, V2 and V3 loop deletion (ΔV1/2/3). The polypeptide also lacks 7 out of 24 N-linked glycosylation sites (dg ΔV1/2/3). The mutants of the gp120 contains similar CD4bs as compared with the glycosylated ΔV1/2/3 glycoprotein and wild-type gp120 (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

33. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Arthos et al. (Cell 1989, Vol. 57, pp. 469-490).

34. Arthos . et al. disclose several recombinant envelope protein comprising V1 or V1V2 or V1V2J4 expressed by E coli. The HIV gp120 polypeptide comprises the glycosylation site alteration (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

35. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Bolmstedt et al. (Journal of Acquired Deficiency Syndromes and Human Retrovirology 1996, Vol. 12, pp. 213-220).

36. Bolmstedt et al. and 14 disclose a recombinant envelope protein of HIV gp160/120 comprising the conserved regions and some point mutations, wherein the gp120 lacks the three N-linked glycans. The mutated HIV gp120 still retain other 3 dimensional structures and discontinuous epitopes as well as CD4 binding domain (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

37. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (P.N.A.S. USA 1992, Vol. 89, pp. 2213-2217).

38. Lee et al. disclose a recombinant envelope protein of HIV gp 120 comprising the conserved regions and some point mutations, wherein each of 24 potential N-linked glycosylation sites in gp120 was individually modified. However, this modification does not affect the CD4 receptor binding or syncytium formation (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

39. Claims 1-4 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bolmstedt et al. (J. Gene Virol. 1991, Vol. 72, pp. 1269-1277).

40. Bolmstedt et al. disclose a recombinant envelope protein of HIV gp 120 comprising the conserved regions, wherein the glycosylation sites at 390 and 447 are mutated. However, these mutations do not change the cell surface CD4-binding activity and other 3 dimensional structure and discontinuous epitopes (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

41. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Essex et al. (WO 93/17705A1).

42. Essex et al. disclose a composition comprising a mutated recombinant envelope protein of HIV gp 120, wherein at least one or multiple N-linked glycosylation sites are deglycosylated. The mutated glycosylation sites are 289, 296, 356, 386, 392, 397, 406 and 463. However, the mutated envelope proteins do not change the CD4-binding region (lines 13 on page 16 to line 28 on page 17) and the mutated gp120 and still maintain 3-dimetional structure of the discontinuous epitope of CD4bs because the molecule is able to bind CD4bs and induce the antibody response in the host (claims 1-14). Therefore, the claimed invention is anticipated by the cited reference.

43. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Earl et al. (J. Virol. 1991, Vol. 65, pp. 31-41).

44. Earl et al. disclose a mutated recombinant envelope protein of HIV gp 120 produced by the vaccine virus vector, wherein the HIV gp120 is truncated at different positions, which change the context of the glycosylation of the protein, but the protein still maintain the CD4 binding sites (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

45. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al. (Nature. 1996, Vol. 384, pp. 179-183).

46. Wu et al. disclose recombinant envelope proteins of HIV gp 120, YUΔC1ΔV1/2ΔC5 or YUΔC1ΔV1/2/3ΔC5, which are mutated with two conserved regions C1 and C5 as well as V1 or V3 variable regions. The mutants of HIV gp120 are expressed by Drosophila Schneider 2 cells without glycosylations. The mutant YUΔC1ΔV1/2ΔC5 contains similar CD4 binding ability (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

47. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Haigwood et al. (AIDS RESEARCH AND HUMAN RETROVIRUSES 1990, Vol. 6, pp. 855-869).

48. Hiaigwood et al. disclose several recombinant envelope proteins of HIV gp 120 polypeptides (Fig. 1 on page 859), which are mutated and expressed in the yeast cells. The said recombinant gp120 is mutated in such as that the polypeptides are capable of expressing intracellularly without glycosylation (lines 11-28 on page 857).The hypervariable regions of this HIV gp120 has been mutated. The modified polypeptides

contain the 3-demisional structure and discontinue epitope CD4bs, which are able to induce immune responses once those polypeptide are injected into the animals (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

49. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Pollard et al. (EMBO Journal 1992, Vol. 11, pp. 585-591).

50. Pollard et al. disclose several recombinant envelope proteins of HIV gp 120 polypeptide comprising the conserved regions and mutated V1, V2 and V3 variable regions. The mutated gp120 polypeptide has different glycosylation sites as compared to the original one. However, the mutated gp120 polypeptide still contains the 3-demisional structure of the discontinue epitope CD4bs and able to induce immune responses once those polypeptide are injected into the animals (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

51. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Lekutis et al. (Journal of Acquired Immune Deficiency Syndromes 1992, Vol. 5, pp. 78-81).

52. Lekutis et al. disclose several recombinant envelope proteins of HIV gp 120 polypeptide comprising the conserved regions and mutated glycosylation sites near the position of the discontinuous CD4 epitopes. The CD4 binding abilities of the mutated 385C/V, 378C/S + 445C/S and 385 C/V + 418 C/S mutants were comparable to , or even better than , that of the wild-type soluble glycoprotein. The more stability of the CD4 binding ability is created by increase the likehood of forming inappropriate disulfide bonds (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for

the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
November 15, 2002

James C. Housel
JAMES HOUSEL 11/18/02
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600